2/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13591346 BIOSIS NO.: 200200220167
Therapeutic activity of **IDEC-114** (anti-CD80) and rituximab (Rituxan(R)) in B-cell lymphoma.
AUTHOR: Hariharan Kandasamy(a); Anderson Darrell(a); Leigh Bryan(a); Berquist Lisa G(a); Murphy Tracey(a); Leonard John E(a); Braslawsky Gary R(a); Hanna Nabil(a)
AUTHOR ADDRESS: (a)IDEC Pharmaceuticals Corp., San Diego, CA**USA
JOURNAL: Blood 98 (11 Part 1):p608a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: **IDEC-114** is a PRIMATIZED(R) antibody that shows specificity to the human CD80 molecule. CD80 is expressed on activated B cells and on B-cell lymphoma. In this study, we evaluated whether **IDEC-114** alone or in combination with rituximab (Rituxan(R)) exhibits an antitumor response against B-cell lymphoma in experimental systems. In vitro cytotoxicity studies showed that **IDEC-114**, like rituximab, kills SB and SKW (CD80+, CD20+) lymphoma cells via antibody dependent cell-mediated cytotoxicity (ADCC). Combination studies using **IDEC-114** and rituximab resulted in enhanced ADCC in vitro. **IDEC-114** also exhibited complement-dependent cytotoxicity (CDC) with CD80 high expression CHO cell transfectants, but failed to mediate CDC with CD80+ B-lymphoma cell lines expressing much lower levels of antigen. These findings indicate that Fc-mediated effector mechanisms of **IDEC-114** are more sensitive than complement when target cells express low density of antigen. Furthermore, in vivo testing of **IDEC-114** in a human B lymphoma/SCID mouse model demonstrated antitumor activity at 100, 200, and 400 mug per injection. The antitumor response observed with **IDEC-114** was comparable to the antitumor response observed with rituximab at the same dose and treatment schedule. Using the same dosing schedule, the combination of **IDEC-114** with rituximab produced superior antitumor activity as compared with either antibody alone. Mice injected with 200 mug of **IDEC-114** and 200 mug of rituximab showed a significantly higher disease-free survival compared with mice injected with either 200 mug of **IDEC-114** ($p<0.005$) or 200 mug of rituximab ($p<0.001$). Furthermore, a significantly greater antitumor response was observed in mice that received the **IDEC-114** /rituximab combination therapy compared with that observed in mice that received 400 mug of **IDEC-114** ($p<0.001$) or 400 mug of rituximab ($p<0.001$) at the same dosing schedule. Overall the results of this study indicate that the combination of **IDEC-114** with rituximab provides a synergistic antitumor response against B-cell lymphoma in vivo.

2/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12465656 BIOSIS NO.: 200000219158
Results of a single-dose, dose-escalating trial of an anti-B7.1 monoclonal antibody (**IDEC-114**) in patients with psoriasis.
AUTHOR: Gottlieb A(a); Abdulghani A; Totoritis M; Lizambri R; Shuey S;

Romano P; Oh C; Chaudhari U; Lebwohl M
AUTHOR ADDRESS: (a)UMDNJ-RWJMS, New Brunswick, NJ**USA
JOURNAL: Journal of Investigative Dermatology 114 (4):p840 April, 2000
CONFERENCE/MEETING: 61st Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA May 10-14, 2000
ISSN: 0022-202X
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

2/7/5 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12032954 EMBASE No: 2003144943
Psoriasis
Lebwohl M.
Dr. M. Lebwohl, Department of Dermatology, Mount Sinai School of Medicine, New York, NY 10029 United States
AUTHOR EMAIL: LebwohlL@aol.com
Lancet (LANCET) (United Kingdom) 05 APR 2003, 361/9364 (1197-1204)
CODEN: LANCA ISSN: 0140-6736
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 99

Recent breakthroughs in the treatment of psoriasis have led to improved understanding of the pathogenesis of this disease. Activation of T lymphocytes leading to release of cytokines results in proliferation of keratinocytes. Several new biological therapies have been developed, which target specific steps in the pathogenesis of psoriasis. With these new treatments, variable degrees of clearing occur. Initial data suggest improved safety over older agents such as methotrexate and ciclosporin, but long-term data are necessary. Enhancements in topical therapy and phototherapy have also increased the armamentarium of treatments available for this disorder.

2/7/6 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11998674 EMBASE No: 2003109630
American Society of Hematology - 44th Annual Meeting and Exposition: 6-10 December 2002, Philadelphia, PA, USA
Talmadge J.E.
J.E. Talmadge, University of Nebraska, Lab. of Transplantation Immunology, Dept. of Pathol./Microbiol. 985660, Omaha, NE 68198-5660 United States
AUTHOR EMAIL: jtalmadg@mail.unmc.edu
IDrugs (IDRUGS) (United Kingdom) 01 FEB 2003, 6/2 (122-126)
CODEN: IDRUF ISSN: 1369-7056
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH

2/7/7 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

11985759 EMBASE No: 2003096191
IDEC-131: IDEC/Eisai
Dumont F.J.

F.J. Dumont, Merck Research Laboratories, Department of Immunology, Room RY80W107, 126 East Lincoln Avenue, Rahway, NJ 07065 United States
AUTHOR EMAIL: francis dumont@merck.com
Current Opinion in Investigational Drugs (CURR. OPIN. INVEST. DRUGS) (United Kingdom) 01 MAY 2002, 3/5 (725-734)
CODEN: CIDRE ISSN: 1472-4472
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 65

2/7/8 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

11922681 EMBASE No: 2003033065
Experimental therapies for psoriasis
Asadullah K.; Volk H.-D.; Friedrich M.; Sterry W.
Dr. K. Asadullah, Corp. Res. Bus. Area Dermatology, Schering AG, D-13342 Berlin Germany
AUTHOR EMAIL: khusru.asadullah@schering.de
Archivum Immunologiae et Therapiae Experimentalis (ARCH. IMMUNOL. THER. EXP.) (Poland) 2002, 50/6 (411-420)
CODEN: AITEA ISSN: 0004-069X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 46

There is a high medical need for better therapies for psoriasis. Based on new insight into the pathophysiology of this frequent immune disease, a number of novel systemic immunomodulatory therapies are currently in clinical development. These include approaches targeting antigen presentation and costimulation, T cell activation and leukocyte adhesion, action of proinflammatory mediators, and modulating the cytokine balance. Although mainly only preliminary data are available so far, these trials contribute to a further understanding of the disease and will eventually lead to new therapeutic options for psoriasis. Moreover, since psoriasis can be considered as a visible model disease for T cell-mediated disorders characterized by a type 1 cytokine pattern in general, such approaches may have impact for other immune disorders as well. Here we review the rationale and the initial clinical data of these important recent experimental therapies.

2/7/9 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

11918533 EMBASE No: 2003027872
Advances in the management of psoriasis: Monoclonal antibody therapies
Mehrabi D.; DiCarlo J.B.; Soon S.L.; McCall C.O.
Dr. C.O. McCall, Department of Dermatology, Emory University, School of Medicine, Atlanta, GA 30322 United States
AUTHOR EMAIL: cmcca05@emory.edu
International Journal of Dermatology (INT. J. DERMATOL.) (United Kingdom) 01 DEC 2002, 41/12 (827-835)
CODEN: IJDEB ISSN: 0011-9059
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 59

Psoriasis is a common skin disorder characterized by erythematous, scaling plaques. Until recently, therapies for this disease have been aimed at reducing keratinocyte proliferation. We have learned that psoriasis is

not primarily a disorder of keratinocyte hyperproliferation, but is an inflammatory disease. This knowledge, especially our current understanding of the role of activated T cells in psoriasis, has led to new therapeutic options and new areas of research. Immunosuppressive agents such as cyclosporine have proven very useful in the treatment of psoriasis, but their use is limited by toxicity. Monoclonal antibodies directed against key components of the inflammatory process have been studied in an attempt to produce safer, more selective immunosuppressive agents. This review summarizes much of the available literature describing the use of monoclonal antibodies in the treatment of psoriasis.

2/7/10 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

11900175 EMBASE No: 2003012299
Treatment targeted to cell surface epitopes
ZELLOBERFLACHEN-EPITOPE ALS THERAPEUTISCHES ZIEL
Mrowietz U.
U. Mrowietz, Klinik fur Dermatologie, Universitat Kiel, Schittenhelmstr. 7, 24105 Kiel Germany
AUTHOR EMAIL: umrowietz@dermatology.uni.kiel.de
H+G Zeitschrift fur Hautkrankheiten (H G Z. HAUTKR.) (Germany) 01 DEC 2002, 77/12 (669-674)
CODEN: ZHKRA ISSN: 0301-0481
DOCUMENT TYPE: Journal ; Review
LANGUAGE: GERMAN SUMMARY LANGUAGE: ENGLISH; GERMAN
NUMBER OF REFERENCES: 38

Expression of a variety of surface epitopes is a characteristic feature of immune cells. Receptors and adhesion molecules are the most predominant ones. It is also characteristic that epitope expression is modulated during cellular activation. In inflammatory skin diseases these structures can be used to define not only the type of cell but also their activity status. The availability of monoclonal antibodies and fusion proteins enabled to target cellular surface epitopes in order to modulate the cellular function as a principle of treatment. In psoriasis receptor-targeted therapy has been developed and tested in a considerable number of clinical trials. However, these approaches revealed that not all the strategies are equally effective. In this review the development of receptor-targeted treatment for skin disorders, mainly psoriasis, is described. Clinical as well as experimental data obtained with the various cornpounds employed are discussed with regard to clinical efficacy, safety and tolerability.

2/7/11 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

11813819 EMBASE No: 2002385879
Clinical and histologic response to single-dose treatment of moderate to severe psoriasis with an anti-CD80 monoclonal antibody
Gottlieb A.B.; Lebwohl M.; Totoritis M.C.; Abdulghani A.A.; Shuey S.R.; Romano P.; Chaudhari U.; Allen R.S.; Lizambri R.G.
Dr. A.B. Gottlieb, Clinical Research Center, UMDNJ-Robert Wood Johnson Med. Sch., 51 French St, New Brunswick, NJ 08901-0019 United States
Journal of the American Academy of Dermatology (J. AM. ACAD. DERMATOL.) (United States) 01 NOV 2002, 47/5 (692-700)
CODEN: JAADD ISSN: 0190-9622
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 35

Pathologic T-cell activation is implicated in psoriasis progression. CD80, a costimulatory molecule involved in T-cell activation, likely plays a key role. **IDEC-114**, an IgGSUB1 anti-CD80 antibody, was evaluated for safety, pharmacokinetics, and preliminary clinical activity in this open-label, single-dose, dose-escalating study in patients with moderate to severe chronic plaque psoriasis. Twenty-four patients received **IDEC-114** (0.05 mg/kg, 0.25 mg/kg, 1 mg/kg, 5 mg/kg, 10 mg/kg, or 15 mg/kg). Psoriasis Area and Severity Index, Physician's Global Psoriasis Assessment, and Psoriasis Severity Scale scores improved in the highest-dose groups. Average plaque thickness and plaque CD3SUP+ and CD8SUP+ T-cell counts decreased in the 10 mg/kg dose group. Adverse events were primarily mild, transient, constitutional symptoms; the most common related events were mild asthenia (29% of patients), chills (25%), and headache (21%). The serum half-life of **IDEC-114** was approximately 13 days. A single dose of **IDEC-114** appears to be safe and well tolerated and has promising clinical activity in psoriasis.

2/7/12 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

11722083 EMBASE No: 2002292687
Biologic therapy for psoriasis: The new therapeutic frontier
Singri P.; West D.P.; Gordon K.B.
Dr. K.B. Gordon, Department of Dermatology, Feinberg School of Medicine, 675 N St Clair St, Chicago, IL 60611 United States
AUTHOR EMAIL: kbg704@northwestern.edu
Archives of Dermatology (ARCH. DERMATOL.) (United States) 2002, 138/5 (657-663)
CODEN: ARDEA ISSN: 0003-987X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 63

Objectives: (1) To develop a clinically useful model with which dermatologists can understand the potential uses of biologic therapy for psoriasis and understand the potential differences among these novel drugs, (2) to discuss the process by which recombinant DNA technology is used to develop rationally designed protein medications along with the potential benefits and difficulties of therapy with biologic agents, and (3) to provide a short review of the medications under development for psoriasis. Data Sources: The pertinent literature was reviewed with particular emphasis on published, randomized, and placebo-controlled trials. Phase 1 and early phase 2 trials were also included in our review when more stringent studies were not available. Studies presented as peer-reviewed abstracts at major conferences were also reviewed. Conclusions: With the development of recombinant DNA techniques, it has become possible to develop new biologic therapies that can be designed to specifically alter physiological responses. These new drugs are in use in many different medical fields and will soon be available for the treatment of dermatological diseases, primarily psoriasis. Dermatologists should be familiar with the potential benefits and risks of these therapies to make rational decisions concerning their use in the treatment of their patients with psoriasis.

2/7/13 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

11587724 EMBASE No: 2002159607
Future of monoclonal antibodies in the treatment of hematologic malignancies

Reff M.E.; Hariharan K.; Braslawsky G.
Dr. M.E. Reff, IDEC Pharmaceuticals Corp, 3010 Science Park Rd, San Diego, CA 92191-9080 United States
AUTHOR EMAIL: MReff@idecpharm.com
Cancer Control (CANCER CONTROL) (United States) 2002, 9/2 (152-166)
CODEN: CACOF ISSN: 1073-2748
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 126

Background: The approval of monoclonal antibodies (MAbs) as antibody-targeted therapy in the management of patients with hematologic malignancies has led to new treatment options for this group of patients. The ability to target antibodies to novel functional receptors can increase their therapeutic efficacy. Methods: The authors reviewed improvements in MAb design to enhance their effectiveness over the existing therapeutic MAb currently approved for treating hematologic malignancies. Results: Three classes of therapeutic MAbs showing promise in human clinical trials for treatment of hematologic malignancies include unconjugated MAb, drug conjugates in which the antibody preferentially delivers a potent cytotoxic drug to the tumor, and radioactive immunotherapy in which the antibody delivers a sterilizing dose of radiation to the tumor. Conclusions: A better appreciation of how MAbs are metabolized in the body and localized to tumors is resulting in the development of new antibody constructs with improved biodistribution profiles.

2/7/14 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

11381104 EMBASE No: 2001396085
Psoriasis: Immunopathology and immunomodulation
Gottlieb A.B.
Dr. A.B. Gottlieb, Clinical Research Center, UMDNJ-Robert Wood Johnson Med. Sch., 51 French Street, New Brunswick, NJ 08901-0019 United States
AUTHOR EMAIL: gottliab@umdnj.edu
Dermatologic Clinics (DERMATOL. CLIN.) (United States) 2001, 19/4 (649-657)
CODEN: DRMCD ISSN: 0733-8635
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 66

Biologics in development for the treatment of moderate to severe plaquetype psoriasis are discussed in this article. Immunomodulators used as therapeutic, pathogenic probes will continue to identify targets that play primary roles in the pathogenesis of psoriasis.

2/7/15 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

11364562 EMBASE No: 2001378774
Therapeutic intervention with inhibitors of co-stimulatory pathways in autoimmune disease
Aruffo A.; Hollenbaugh D.
A. Aruffo, Immunol./Inflammation Drug Discovery, B.-M. Squibb Pharmaceut. Res. Inst., PO Box 5400, Princeton, NJ 08543 United States
AUTHOR EMAIL: alejandro.aruffo@bms.com
Current Opinion in Immunology (CURR. OPIN. IMMUNOL.) (United Kingdom) 01 DEC 2001, 13/6 (683-686)
CODEN: COPIE ISSN: 0952-7915

DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 28

Many humanized antibodies and fusion proteins targeting T-cell co-stimulatory molecules are now in late-stage clinical development (phase II, phase III) or have recently completed phase III clinical trials. Both Amevive, an LFA-3-Ig fusion protein targeting CD2, and Xanelim, a humanized anti-CD11a antibody, have shown efficacy in pivotal phase III trials in patients with plaque psoriasis. These new medicines are poised to enter clinical use in 2002.

2/7/16 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

11326733 EMBASE No: 2001338888
Alefacept. Antipsoriatic
Sorbera L.A.; Revel L.; Fernandez R.
L.A. Sorbera, Prous Science, P.O. Box 540, 08080 Barcelona Spain
Drugs of the Future (DRUGS FUTURE) (Spain) 2001, 26/6 (527-532)
CODEN: DRFUD ISSN: 0377-8282
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 32

2/7/17 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

11186618 EMBASE No: 2001200214
IDEC-114 IDEC
Schopf R.E.
R.E. Schopf, Johannes Gutenberg University, Department of Dermatology, 55101 Mainz Germany
AUTHOR EMAIL: schopf@hautlink.klink.uni-mainz.de
Current Opinion in Investigational Drugs (CURR. OPIN. INVEST. DRUGS) (United Kingdom) 2001, 2/5 (635-638)
CODEN: CIDRE ISSN: 0967-8298
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 28

IDEC is developing a PRIMATIZED-anti-B7 antibody (**IDEC-114**) for the treatment of autoimmune and inflammatory diseases, such as psoriasis and rheumatoid arthritis. It is currently undergoing phase II trials in patients with psoriasis. A randomized, blind, placebo-controlled, multiple-dose phase II study was initiated in January 2001 to evaluate the potential clinical activity and safety of **IDEC-114** in patients with moderate-to-severe psoriasis. The antibody targets the B7 antigen on the surface of antigen-presenting cells that normally interact with T-cells to initiate an immune response. Antibodies directed at B7 may be useful in preventing unwanted immune responses in autoimmune diseases such as systemic lupus erythematosus, idiopathic thrombocytopenic purpura as well as transplant rejection. PRIMATIZED antibodies, genetically engineered from cynomolgus macaque monkey and human components, are structurally indistinguishable from human antibodies. They may, therefore, be less likely to cause adverse reactions in humans, making them potentially suited for long-term, chronic treatment. IDEC has signed an antibody humanization patent licensing agreement with Protein Design Labs. IDEC is also collaborating with Mitsubishi-Tokyo (formerly Mitsubishi Kasei) on the development of this antibody.

2/7/18 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

11183476 EMBASE No: 2001197890
hu1124. Antipsoriatic, treatment of transplant rejection
Sorbera L.A.; Leeson P.A.; Graul A.; Revel L.
L.A. Sorbera, Prous Science, P.O. Box 540, 08080 Barcelona Spain
Drugs of the Future (DRUGS FUTURE) (Spain) 2001, 26/3 (232-238)
CODEN: DRFUD ISSN: 0377-8282
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 29
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TEM:OS  - DIALOG OneSearch
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         (c) 2003 BIOSIS
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removal, customized scheduling. See HELP ALERT.
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         (c) 2003 Elsevier Science B.V.
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changed.  Please see HELP NEWS 155.
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? s (idec(w)114)
            737  IDEC
          49019  114
      S1     22  (IDEC(W)114)
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      S2     18  RD S1 (unique items)
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 2/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

14225485   BIOSIS NO.: 200300219514
Biotherapy: A novel approach in the treatment of psoriasis.
AUTHOR: Agarwal Ravindra(a); Vij Nitika; Katare Om P
AUTHOR ADDRESS: (a)University Institute of Pharmaceutical Sciences, Panjab
  University, Chandigarh, 160 014, India**India
JOURNAL: Drugs of the Future  27 (11):p1071-1077 November 2002 2002
MEDIUM: print
ISSN: 0377-8282
DOCUMENT TYPE: Literature Review
RECORD TYPE: Citation
LANGUAGE: English


 2/7/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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13781038   BIOSIS NO.: 200200409859
Antibody combination of IDEC-114 (anti-CD80) and rituximab
  (Rituxan(R)) in B-cell lymphoma therapy.
AUTHOR: Hariharan Kandasamy(a); Berquist Lisa G(a); Murphy Tracey(a); Hanna
  Nabil(a); Braslawsky Gary R(a)
AUTHOR ADDRESS: (a)IDEC Pharmaceuticals Corp., San Diego, CA**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual
Meeting  43p910 March, 2002
MEDIUM: print
CONFERENCE/MEETING: 93rd Annual Meeting of the American Association for
Cancer Research  San Francisco, California, USA  April 06-10, 2002
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English
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12011094 EMBASE No: 2003121668
First-line and maintenance treatment with **rituximab** for patients with indolent non-Hodgkin's **lymphoma**
Hainsworth J.D.
Dr. J.D. Hainsworth, Sarah Cannon Cancer Center, 250 25th Ave North, Nashville, TN 37203 United States
Seminars in Oncology (SEMIN. ONCOL.) (United States) 2003, 30/1
SUPPL. 2 (9-15)
CODEN: SOLGA ISSN: 0093-7754
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 18

The chimeric **human**-mouse anti-CD20 monoclonal antibody **rituximab** has durable single-agent activity in patients with relapsed and refractory indolent non-Hodgkin's **lymphoma**. The focus of this report is a phase II trial evaluating the efficacy of single-agent **rituximab** as first-line therapy in patients with indolent **lymphoma** and scheduled maintenance treatment in prolonging duration of remission. Patients received a 4-week course of standard **rituximab** (375 mg/mSUP2 intravenously weekly x 4). Those achieving objective response or stable disease then received maintenance courses of standard **rituximab** every 6 months, for a maximum of four **rituximab** courses. Of 62 patients entered in the trial, 61% had follicular **lymphoma** while 39% had small lymphocytic **lymphoma** (SLL). At 6 weeks, 28 of 60 evaluable patients (47%) had an objective response. The response rate improved to 73% (37% complete response) following maintenance **rituximab** therapy and was similar in patients with follicular **lymphoma** and SLL (76% v 70%, respectively). Median progression-free survival for the entire group was 34 months. Single-agent therapy was well tolerated and maintenance **rituximab** was administered without grade 3/4 toxicity. Because of the higher activity of **rituximab** in this study compared with previous results in patients with relapsed or refractory SLL, a second phase II trial of identical design but limited to patients with SLL and chronic lymphocytic leukemia was initiated. Forty-four patients entered this second trial and, at present, 27 continue to receive maintenance courses of **rituximab**. The current response rate is 56% (8% complete responses). In summary, **rituximab** appears highly active as first-line single-agent therapy for indolent non-Hodgkin's **lymphoma** and responses may be improved with maintenance courses of **rituximab**. Results suggest a higher response rate to **rituximab** when used as first-line compared with second/third-line treatment, particularly in the subset of patients with SLL and chronic lymphocytic leukemia. Further follow-up will provide important information regarding the impact of first-line and maintenance **rituximab** on progression-free survival in patients with indolent non-Hodgkin's **lymphoma**.

6/7/76 (Item 51 from file: 73)
DIALOG(R)File 73:EMBASE

12011093 EMBASE No: 2003121667
The mechanisms of action of **rituximab** in the elimination of tumor cells
Johnson P.; Glennie M.
Prof. P. Johnson, CR UK Oncology Unit, Southampton General Hospital, Southampton, SO16 6YD United Kingdom
Seminars in Oncology (SEMIN. ONCOL.) (United States) 2003, 30/1
SUPPL. 2 (3-8)
CODEN: SOLGA ISSN: 0093-7754

DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 35

The anti-CD20 chimeric monoclonal antibody **rituximab** kills B cells by multiple mechanisms, including complement-dependent cytoxicity, antibody-dependent cellular cytotoxicity, and induction of apoptosis. **Rituximab** can also sensitize cells to the effects of chemotherapy. To optimize treatment of non-Hodgkin's **lymphoma** and improve response rates, a fuller understanding of these mechanisms and their relative contributions to **clinical** efficacy is required. Therefore, this has been an area of active research in recent years. Preclinical studies have established that the **human** Fc region of **rituximab** is important in mobilizing antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity effector mechanisms. In addition, molecular consequences of CD20 binding, including redistribution of membrane lipid "rafts," activation of src kinases, phospholipases and caspases, and down-regulation of interleukin-10, have been identified. **Clinical** studies have also identified differences in patients' responses to **rituximab** associated with Fc receptor polymorphisms, and increases in enzymes involved in apoptotic pathways have been seen in the lymphocytes of patients following **rituximab** treatment. This article reviews the current understanding of the mechanisms of **rituximab** cell killing in the light of the latest **clinical** and preclinical data.

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Set	Items	Description
S1	3451	(IDEC(W)114 OR RITUXIMAB)
S2	2237	S1 AND LYMPHOMA?
S3	1395	S2 AND (CLINICAL OR VIVO)
S4	1338	S3 AND HUMAN
S5	132	S4 AND PY=2003
S6	113	RD S5 (unique items)

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